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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/460,186	06/02/1995	REID VON BORSTEL	1331-138	5103

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EXAMINER

KHARE, DEVESH

ART UNIT PAPER NUMBER

1623

DATE MAILED: 03/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

08/460,186

Applicant(s)

VON BORSTEL ET AL.

Examiner

Devesh Khare

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 February 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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Applicant's response to the advisory action filed on 02/03/2006 is acknowledged. In response to applicant's request to issue a non-final action under Rule 129(a) filing on 2/23/2005 has been considered. The finality of the Office Action dated 2/23/2004 has been withdrawn. The IDSs' dated 2/21/04 and 1/12/06 had been considered in the previous office actions.

In response to applicant's remarks to rejections of Office Action dated 2/23/2004 include:

Obviousness double patenting rejections: which have been withdrawn.

103(a) rejections: which have been withdrawn.

An action on the merits of claims 1-25 is contained herein below.

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-25 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over U.S. Patent No. 6,329,350 ('350) and applicant's other U.S. Patents of same scope as following:

5,346,708

5,470,838

5,583,117

5,691,320

5,736,531

5,770,582

5,968,914

6,020,320

6,020,322

6,054,441

8,060,459

6,103,701

6,232,298

6,255,290

6,258,795

6,274,563

6,297,222

6,306,834

6,316,426

6,344,447

6,348,451

6,403,565

6,417,170

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6,465,440

6,472,378

6,743,782

Although the conflicting claims are not identical, they are not patentably distinct from each other because the '350 patent claims a method in claims 1-7 for treating cancer consisting essentially of administering to an animal a therapeutically effective amount of a pyrimidine nucleotide precursor which is a pyrimidine nucleoside or prodrug thereof wherein said methods are encompassed by or has substantial overlap with the methods of the instant claims. The instant methods are drawn for preventing or treating toxicity due to a pyrimidine analog comprising administering to an animal a pharmaceutically effective amount of an acylated derivative of a non-methylated pyrimidine nucleoside. It would be obvious to select the pyrimidine nucleoside or prodrug thereof set forth in the claims of the issued patent for preventing or treating toxicity due to a pyrimidine analog of instant claims because the composition containing an acylated derivative of a non-methylated pyrimidine nucleoside would be considered an inherent property of the pyrimidine nucleosides for the treatment of cancer as well as preventing or treating toxicity due to a pyrimidine analog in an animal, absent any clear and convincing evidence and/or arguments to the contrary.

The molecule comprising pyrimidine nucleosides may well be varied in terms of its inherent activity, in this case to accomplish prevention or treatment of toxicity due to a

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pyrimidine analog comprising administering to an animal a pharmaceutically effective amount of an acylated derivative of a non-methylated pyrimidine nucleoside.

The examiner notes the instant claims; the '350 patent and said U.S. Patents of applicants, claims do indeed substantially overlap because the method in the instant claims and the said patents are deemed same or substantial same and this obviousness-type double patenting rejection is necessary to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees.

Therefore the claims are co-extensive.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

35 U.S.C. 112, first paragraph rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling effects of uridine and cytidine derivatives such as triacetyluridine (tau); octanoyl uridine; diacetyldeoxycytidine; and palmitoyldeoxycytidine (specification: Examples, pages 60-106), does not reasonably provide enablement for preventing or treating toxicity due to a pyrimidine nucleoside analog comprising administering to an animal a pharmaceutically effective amount of an acylated derivative

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of a non-methylated pyrimidine nucleoside. The selection of compounds of an acylated derivative of a non-methylated pyrimidine nucleoside is too broad as the compounds disclosed in Examples, pages 60-106. In the absence of which of an acylated derivative of a non-methylated pyrimidine nucleoside of claim 1 and in the absence of data disclosing the effectiveness of an acylated derivative of a non-methylated pyrimidine nucleoside of claim 1 for preventing or treating toxicity in an animal, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- (1) The nature of the invention;
- (2) The state of the prior art;
- (3) The predictability or lack thereof in the art;
- (4) The amount of direction or guidance present;
- (5) The presence or absence of working examples;
- (6) The breadth of the claims;
- (7) The quantity of experimentation needed; and
- (8) The relative skill of those in the art.

THE NATURE OF THE INVENTION

The nature of the invention in claims 1-25 is a method for preventing or treating toxicity due to a pyrimidine nucleoside analog comprising administering to an animal a

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pharmaceutically effective amount of an acylated derivative of a non-methylated pyrimidine nucleoside of claim 1.

THE STATE OF THE PRIOR ART

The instant claimed a method for preventing or treating toxicity due to a pyrimidine nucleoside analog comprising administering to an animal a pharmaceutically effective amount of an acylated derivative of a non-methylated pyrimidine nucleoside. The following references are cited to show the state of the prior art:

Martin et al., Cancer Res., 1982.

Sommadossi et al. Antimicrobial Agents and Chemotherapy, 1988.

(the prior art references are provided in the Office Action dated 2/23/2004).

Martin et al. discloses that administering exogenous uridine can reduce the toxicity of 5-FU and actually "rescue" mice from toxic dose of 5-FU.

Sommadossi et al. also discloses that uridine administration can reduce the toxicity of a pyrimidine nucleoside analog, AZT.

THE PREDICTABILITY OR LACK THEREOF IN THE ART

There would be little predictability in the art of which modifications may be made to an acylated derivative of a non-methylated pyrimidine nucleoside, which would retain its capability to prevent or treat toxicity due to a pyrimidine nucleoside analog comprising administering to an animal. The nature of the pharmaceutical arts is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that

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the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. In the absence of which Markush groups of the acylated derivative of a non-methylated pyrimidine nucleoside depicted in claim 1 are being effective for the said prevention or treatment, there is no umbrella coverage springing forth from the claimed compounds for the said method.

THE AMOUNT OF DIRECTION OR GUIDANCE PRESENT

The acylated derivative of a non-methylated pyrimidine nucleoside of claim 1 may encompass a great number of compounds having various Markush groups, however, without some guidance as to what specific changes may be made to the instant compound effective for the said treatment, there would be little predictability in making and/or using such compounds. For example, there is no guidance as to which Markush groups may be selected to the specific compound that would retain its capability to prevent or treat toxicity due to a pyrimidine nucleoside analog comprising administering to an animal. One skilled in the art would not expect any modifications of the instant compound, which is effective for the said method.

THE PRESENCE OR ABSENCE OF WORKING EXAMPLES

The working Examples (pages 60-106) disclose the oral administration of TAU, Oct-U, DadC and PdC to ameliorate hematologic toxicity of 5-FU in mice.

BREATH OF THE CLAIMS

The breadth of the claims is that a method for preventing or treating toxicity due to a pyrimidine nucleoside analog comprising administering to an animal a pharmaceutically effective amount of an acylated derivative of a non-methylated pyrimidine nucleoside.

THE QUANTITY OF EXPERIMENTATION NEEDED

The quantity of experimentation needed is undue experimentation. One skill in the art would need to determine what listed compounds from a broadly claimed acylated derivative of a non-methylated pyrimidine nucleoside of claim 1 would be effective to use in a method for preventing or treating toxicity due to a pyrimidine nucleoside analog comprising administering to an animal a pharmaceutically effective amount of an acylated derivative of a non-methylated pyrimidine nucleoside.

THE LEVEL OF SKILL IN THE ART

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity **in an animal**. Thus the specification fails to provide sufficient support of the broad use of the acylated derivative of a non-methylated pyrimidine nucleoside of claim 1 because no specific compound is provided. As a result necessitating one of skill to perform an exhaustive search for which compound can be prepared in order to practice the claimed invention.

Genentech Inc. v Novo Nordisk A/S (CA FC) 42 USPQ 2d 1001, states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

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Therefore, in view of the Wands factors discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which compound out of a broadly claimed acylated derivative of a non-methylated pyrimidine nucleoside of claim 1 is effective in the method encompassed in the instant claims, with no assurance of success.


Any inquiry concerning this communication or earlier communications from the

Examiner should be directed to Devesh Khare whose telephone number is (571)272-0653. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang, Supervisory Patent Examiner, Art Unit 1623 can be reached at (571)272-0627. The official fax phone numbers for the organization where this application or proceeding is assigned is (703) 308-4556 or 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Devesh Khare, Ph.D.,J.D.
Art Unit 1623
March 6, 2006


Anna Jiang, Ph.D.
Supervisory Patent Examiner
Art Unit 1623